

Applicant : Pilarski et al
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AMENDMENTS TO THE CLAIMS

Claims 1-17, 21-23, 27-34, 38-41, 45-50 and 88-90 are pending in this application.

Claims 1-20, 22, 29, 31, and 45-48 are being canceled, and claims 21, 28, 30, 32, 34, 38 - 39, 49 and 88 are amended. After the amendments, claims 21, 23, 27 - 28, 30, 32 - 34, 38 - 41, 49 - 50, 88 - 90, and 106 - 107 will be pending.

This listing of claims replaces all prior versions and listings of claims in the application.

Claims Listing:

1.-20. (Cancelled)

21. (Currently amended) A method to detect expression of HAS1 isoenzyme variants comprising:

i) mixing a cell or sample of cell population from a human with reverse transcriptase in conditions enabling conversion of mRNA to DNA templates thereby generating cDNA templates;

ii) mixing said cDNA with oligonucleotide primers SEQ ID NO:9 and SEQ ID NO: 10; specific for HAS1, whereby primers are selected so as to enable generation of amplified fragments of differing size for each HAS1 isoenzyme variant;

a. Reacting said mixture with enzymes and compounds to enable specific fragments of DNA to be increased in number;

b. Detecting the presence of an increased number of resulting DNA fragments of particular size associated with the presence of particular HAS1 isoenzyme variants.

22. (Cancelled)

23. (Previously presented) The method of claim 21 wherein the isoenzyme variant is HAS1Va.

24.-26. (Withdrawn)

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27. (Previously presented) The method of claim 21 wherein the process is performed using a microfluidic device.

28. (Currently amended) A method to detect expression of HAS1Va isoenzyme variant in a cell or cell population comprising detection of single nucleotide conversion of base 924 of the HAS1Va cDNA from a cytosine to a thymidine residue ~~polymorphism of the HAS1Va gene.~~

29. (Cancelled)

30. (Currently amended) A method to detect disease resulting from genetic instability comprising characterizing HAS ~~isoenzyme~~ and isoenzyme variant expression in a cell or cell population.

31. (Canceled).

32. (Currently amended) The method of claim 30 wherein characterizing of HAS ~~isoenzyme~~ and isoenzyme variants comprises detection of HAS1 isoenzyme variants.

33. (Previously presented) The method of claim 30 wherein the cell or cell population is selected from the group comprising blood, B-cells, CD 19.sup.+ B cells, CD 19.sup.+ peripheral blood mononuclear cells and bone marrow plasma cells.

34. (Currently amended) The method of claim ~~29-28~~ or 33 wherein the characterization of HAS isoenzyme variant expression comprises detection of HAS1Va.

35 - 37 (Withdrawn)

38. (Currently amended) A method to detect susceptibility to disease resulting from genetic instability comprising characterizing of HAS ~~isoenzyme~~ or isoenzyme variant expression in a cell or cell population.

39. (Currently amended) The method of claim 38 wherein characterization of HAS ~~isoenzyme~~ and isoenzyme variants comprises detection of HAS1 isoenzyme variants

40. (Previously presented) The method of claim 38 wherein the cell or cell population is selected from the group comprising blood, B-cells, CD 19.sup.+ B cells, CD 19.sup.+ peripheral blood mononuclear cells and bone marrow plasma cells.

41. (Previously presented) The method of claim 40 wherein the characterization of HAS isoenzyme variant expression comprises detection of HAS1Va.

42 - 44 (Withdrawn)

45 - 48 (Cancelled)

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49. (Currently amended) A method to determine the likelihood of poor clinical outcome in a human suffering from multiple myeloma comprising characterizing HAS ~~isoenzyme~~ ~~or~~-isoenzyme variant expression in a cell or cell population.

50. (Previously presented) The method of claim 49 wherein the cell or cell population is selected from the group comprising blood, B-cells, CD 19.sup.+ B cells, CD 19.sup.+ peripheral blood mononuclear cells and bone marrow plasma cells.

51.-87. (Withdrawn).

88. (Currently amended) A method to monitor malignant cells in a human comprising detection of HAS ~~isoenzymes~~ ~~or~~-isoenzyme variants in a sample of cells or cell population from a human.

89. (Previously presented) The method of claim 88 wherein the human is suffering from Multiple Myeloma.

90. (Previously presented) The method of claim 88 wherein the human is suffering from Waldenstrom's Macroglobulemia.

106. (New) The method of claim 30 wherein the disease resulting from genetic instability is selected from the group comprising cancer and Multiple Myeloma

107. (New) A method to detect susceptibility to disease comprising detection of conversion of base 924 of the HAS1Va cDNA from a cytosine to a thymidine residue.